

CLAIMS

The invention claimed is:

1. A method for producing a compound that regulates telomerase activity, comprising:
 - a) obtaining a preparation of mammalian telomerase enzyme that is at least ~2000-fold more pure than an extract of cells from adenovirus-transformed kidney cell line (293 cells), wherein the telomerase enzyme contains telomerase RNA component, and has a molecular weight of 200-2000 kDa;
 - b) combining the preparation with a test compound;
 - c) determining telomerase activity of the enzyme in the presence of the test compound;
 - d) identifying the compound as being a regulator of telomerase if the telomerase activity measured in step c) is affected by the presence of the compound; and then
 - e) producing the compound if it is identified as being a regulator of telomerase in step d).
2. A method for producing a compound that regulates telomerase activity, comprising:
 - a) identifying the compound as being a regulator of telomerase; and then
 - b) producing the compound if it is identified as being a regulator of telomerase in step a);wherein the compound has been identified as a regulator of telomerase by a process comprising:
 - i) obtaining a preparation of mammalian telomerase enzyme that is at least ~2000-fold more pure than an extract of cells from adenovirus-transformed kidney cell line (293 cells), wherein the telomerase enzyme contains telomerase RNA component, and has a molecular weight of 200-2000 kDa;
 - ii) combining the preparation with a test compound;
 - iii) determining telomerase activity of the enzyme in the presence of the test compound;
 - iv) identifying the compound as being a regulator of telomerase if the telomerase activity measured in step iii) is affected by the presence of the compound.

3. The method of claim 1 or claim 2, wherein the telomerase preparation was obtained by a process in which a solution containing telomerase activity was combined with an oligonucleotide having specific activity for mammalian telomerase; and then protein was collected that had bound the oligonucleotide.
4. The method of claim 3, wherein the oligonucleotide comprises a retrievable label such as biotin.
5. The method of claim 3, wherein the solution that was combined with the oligonucleotide had been obtained by preparing an enriched solution from a cell expressing telomerase, whereby telomerase enzyme in the enriched solution was separated from other proteins expressed by the cell.
6. The method of claim 1 or claim 2, wherein the process used to prepare the telomerase comprised combining a fraction containing telomerase enzyme with an anion exchange matrix, and collecting protein that bound the matrix.
7. The method of claim 1 or claim 2, wherein the process used to prepare the telomerase comprised combining a fraction containing telomerase enzyme with a cation exchange matrix (such as a heparin matrix), and collecting protein that bound the matrix.
8. The method of claim 1 or claim 2, wherein the process used to prepare the telomerase comprised combining a fraction containing telomerase enzyme with an intermediate selectivity matrix, and collecting protein that bound the matrix; wherein the intermediate selectivity matrix had at least one of the following substituents: hydroxyapatite, a polyamine (such as spermine or spermidine), poly guanylic acid, a divalent metal ion (such as Ni^{++}), a positively charged poly-amino acid (such as poly-L-lysine), a positively charged enzyme (such as histone), or aminophenyl-boronic acid.

9. The method of claim 1 or claim 2, wherein the process used to prepare the telomerase comprised separating a fraction containing the telomerase enzyme by gel filtration chromatography or gradient centrifugation that separates molecules > 200 kDa.
10. The method of claim 3, wherein the oligonucleotide contains a sequence that binds specifically to telomerase RNA component.
11. The method of claim 10, wherein the oligonucleotide contains the sequence of oligo 5 (SEQ. ID NO:3).
12. The method of claim 3, wherein the oligonucleotide contains a sequence that is specifically recognized by telomerase protein.
13. The method of claim 12, wherein the oligonucleotide contains the sequence (TTAGGG)₃ (SEQ. ID NO:6).
14. The method of claim 12, wherein the oligonucleotide does not contain the sequence (TTAGGG)₃ (SEQ. ID NO:6).
15. The method of claim 12, wherein the oligonucleotide contains the sequence of M2/TS (SEQ. ID NO:8).
16. The method of claim 12, wherein the telomerase preparation is at least ~20,000 fold more pure than the cell extract.
17. The method of claim 1 or claim 2, wherein the telomerase preparation is between ~3,000 and ~60,000 fold more pure than the cell extract.
18. The method of claim 1 or claim 2, wherein the telomerase protein is human.
19. The method of claim 1 or claim 2, wherein the telomerase preparation has measurable telomerase activity in 0.2 µg of protein when quantified in a telomere primer elongation assay in which ³²P-labeled primer extensions are separated on a gel and detected using a phosphoimager screen.

20. The method of claim 1 or claim 2, wherein telomerase core enzyme is present in the preparation at a concentration of at least $3 \times 10^{-10} \text{ mol L}^{-1}$.
21. The method of claim 1 or claim 2, wherein telomerase core enzyme is present in the preparation at a concentration of at least $2 \times 10^{-9} \text{ mol L}^{-1}$.
22. The method of claim 1 or claim 2, wherein the telomerase activity is determined by a primer elongation assay.
23. The method of claim 1 or claim 2, wherein the telomerase activity is determined in by a dot blot assay.
24. The method of claim 1 or claim 2, whereby the compound is identified as being an inhibitor of telomerase.
25. The method of claim 1 or claim 2, whereby the compound is identified as being an activator of telomerase.